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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/980,243	11/29/2001	Wolf-Dietrich Freund	Le A 33 469	1294

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EXAMINER	
ANDERSON, REBECCA L	
ART UNIT	**PAPER NUMBER**
1626	7

DATE MAILED: 03/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/980,243	FREUND ET AL.	
	Examiner	Art Unit	
	Rebecca L Anderson	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *23 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11 and 15-21* is/are pending in the application.

4a) Of the above claim(s) *6-10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5, 11 and 15-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *1* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-11 and 15-21 are currently pending in the instant application. Claims 6-10 are withdrawn from further consideration as being drawn to a non-elected invention. Claims 19-21 are rejected and claims 1-5, 11 and 15-18 are provisionally rejected.

Election/Restrictions

Applicant's election with traverse of Group IX, as found on page 2 of Paper No. 6, mailed 23 January 2003 is acknowledged. The traversal is on the ground(s) that the examiner has misinterpreted the rules concerning unity of invention in the context of a Markush claim and has incorrectly identified the technical feature in common with each of the inventions. Applicant also provides a structure on page 4 of the response to the restriction requirement which applicant considers the special technical feature that defines a contribution which each of the inventions, considered as a whole, makes over the prior art. This is not found persuasive because the claims herein lack unity of invention under PCT rule 13.1 and 13.2 since the compounds defined in the claims lack a significant structural element qualifying as the special technical feature that defines a contribution over the prior art and the alternatives (the substituents) on the common structure do not all belong to an art recognized class of chemical compounds (i.e. R2 can contain a morpholine, a piperazine or an alkyl group). The compounds claimed contain a cyclohexyl benzimidazole, which does not define a contribution over the prior art (as can be seen by the compounds on page 4 of EP 0 725 064 A1). The substituents on the cyclohexyl benzimidazole vary extensively and when taken as a whole result in vastly different compounds. Accordingly, unity of invention is considered

to be lacking and restriction of the invention in accordance with the rules of unity of invention is considered to be proper. Additionally, even if the structure on page 4 of applicants response was the technical feature that all of the inventions have in common, this would still not be a special technical feature that defines a contribution which each of the inventions, considered as a whole, makes over the prior art because this feature is well known in the art as can be seen by US Patent No. 5, 395, 840 (columns 24) and US Patent No. 5, 935, 983 (column 2).

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of an ischaemic brain disorder does not reasonably provide enablement for the prophylaxis of an ischaemic brain disorder. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,

3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case, applicants are claiming a method of treating and preventing an ischaemic brain disorder (claim 19), such as stroke, reperfusion damage or brain trauma (claim 21). The nature of pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face. As defined the claims read on treating and preventing all ischaemic brain disorders which is broader than the enabling disclosure. The compounds which are disclosed in the specification, which have data regarding the treatment of ischaemic brain disorders (pages 26-29), have no pharmacological data regarding the prevention of ischaemic brain disorders, i.e. the specification is short of any data (animal models, *in vitro* or *in vivo* testing) in regards to the prevention of ischaemic brain disorders. Therefore, claims 19-21 are rejected under 35 U.S.C. 112, first paragraph. This rejection can be overcome by deleting the phrase "or prophylaxis" from claim 19.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the

unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-5, 11 and 15-18 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6, 8, 16, 21-28, 30-34 and 36-40 of copending Application No. 09980242. Although the conflicting claims are not identical, they are not patentably distinct from each other because:

Applicants instant claims 1-4 and 11 are directed to products of the general formula (I) wherein A, D, E and G are CH, R1 is C(O)-NR4R5 wherein R4 and R5 are H or (C1-C6)alkyl, R2 is 4-R7-piperazin-1-yl, R7 is H, (C1-C6)alkyl, etc., R3 is optionally substituted phenyl or naphthyl and L1 and L2 are hydrogen, halogen hydroxyl, carboxyl,

etc.. Claim 5 specifically discloses (S)-N-{{(1R,2R)-2-{4-{[2-(4-Methyl-piperazin-1-yl)-benzimidazol-1-yl]methyl}-phenyl}-cyclohex-1-yl} carbonyl}-phenylglycinamide. Claim 5 and claims 15-18 are drawn to a process for preparing compounds of the general formula (I) using the compounds of formulas (II), (III), (IV), (V) and (VI) or (IIIa), (VII), (VIII), (IX) and (X). Claims 15-18 limit the substituents on the compounds, i.e. T is methyl or tert-butyl, V is halogen, mesylate or tosylate, V is bromine, and Y is chlorine or bromine.

The claims 1-6, 16, 21-28 and 36-41 of copending Application No. 09980242 disclose products of the general formula (I) wherein wherein A, D, E and G are CH or nitrogen atoms, more specifically wherein A, D and E are CH and G is CH or nitrogen (claim 3), R1 is CH2-OH or C(O)-NR4R5, more specifically wherein R1 is C(O)-NR4R5 (claim 3) wherein R4 and R5 are H or (C1-C6)alkyl, R2 is (C3-C8)-cycloalkyl, (C1-C8)-alkyl, a 4 to 8 membered saturated heterocycle, more specifically wherein R2 is 4-R7-piperazin-1-yl (claim 3), R7 is H, (C1-C6)alkyl, etc., R3 is phenyl, naphthyl, pyrimidinyl, pyridyl, furyl or thienyl, more specifically wherein R3 is phenyl or pyridyl (claim 3) and L1 and L2 are hydrogen, halogen hydroxyl, carboxyl, etc., more specifically wherein L1 and L2 are hydrogen (claim 3) . Claim 8 and claims 30-34 are drawn to a process for preparing compounds of the general formula (I) using the compounds of formulas (II), (III), (IV), (V) and (VI) or (IIIa), (VII), (VIII), (IX) and (X).

The difference between the instant claims and the claims of copending Application No. 09980242 is that certain claims in copending Application No. 09980242

disclose specific stereochemistry for the compounds as claimed, G can represent CH or a nitrogen atom and R3 can be phenyl or pyridyl.

However, it would have been obvious to someone of ordinary skill in the art, when faced with co-pending Application No. 09980242 to prepare compounds wherein G is CH, R3 is phenyl and compounds with specific stereochemistry when the specification in the instant application discloses on page 4 that the compounds according to the invention can occur in different stereoisomeric forms. A specific example is the compound of example 5, which is (S)-N-{{(1R,2R)-2-{4-{[2-(4-Methyl-piperazin-1-yl)-benzimidazol-1-yl]methyl}-phenyl}-cyclohex-1-yl} carbonyl}-phenylglycinamide, page 43. Therefore the claims at issue in the instant application specifically encompass compounds with the specific stereochemistry as found in the claims of copending Application No. 09980242. In regards to the substituent G and R3, the copending application discloses the compound of example 5, page 55, (S)-N-{{(1R,2R)-2-{4-{[2-(4-Methyl-piperazin-1-yl)-benzimidazol-1-yl]methyl}-phenyl}-cyclohex-1-yl} carbonyl}-phenylglycinamide, which is a compound under the instant claims that has the substituent G as CH and R3 is phenyl. This specific example in the copending specification shows a preference toward compounds where G is CH. Therefore the claims in the copending application specifically encompass compounds wherein G is CH. The motivation to make the instantly claimed compounds is to prepare other compounds that are useful for the treatment of ischeamic braid disorders.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Objections

Claims 1-5, 11 and 15-21 are objected to as containing non-elected subject matter, but would appear allowable if rewritten to include only the elected subject matter as found on page 2 of Paper No. 6, applicants response to the restriction requirement, rewritten to overcome the 35 U.S.C. 112 1st paragraph rejection and rewritten to overcome the provisional obvious type double patenting rejection or providing a terminal disclaimer to overcome the provisional obvious type double patenting rejection.

Conclusion

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rebecca L. Anderson whose telephone number is (703) 605-1157. Mrs. Anderson can normally be reached Monday through Friday 7:00AM to 3:30PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. Joseph McKane, can be reached at (703) 308-4537.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone numbers are (703) 308-1235 and (703) 308-0196.

A facsimile center has been established. The hours of operation are Monday through Friday, 8:45AM to 4:45PM. The telecopier numbers for accessing the facsimile machine are (703) 308-4242, (703) 305-3592, and (703) 305-3014.

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